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Pulmonary Function is Associated with Distal Aortic Calcium, not Proximal Aortic Distensibility. MESA Lung Study

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Abstract

Forced expiratory volume in one second strongly predicts mortality from cardiovascular disease. FEV_1 has been associated with aortic stiffness a strong independent predictor of cardiovascular mortality. However, the anatomical site and possible mechanisms linking aortic stiffness and lung function are unknown. We therefore examined if FEV_1 and CT percent emphysema were associated with calcification of the abdominal aorta or reduced distensibility of the proximal thoracic aorta.

The Multi-Ethnic Study of Atherosclerosis (MESA) measured aortic calcification on cardiac and abdominal CT scans and proximal aortic distensibility using magnetic resonance among participants aged 45–84 years without clinical cardiovascular disease. Spirometry was measured following ATS/ERS guidelines and percent emphysema was measured in the lung fields of cardiac CT scans. Multivariate analyses adjusted for age, sex, race/ethnicity and cardiovascular risk factors.

Of 1,917 participants with aortic distensibility measures, 13% were current and 38% were former smokers. Eighteen percent had airflow limitation without asthma. FEV_1 was associated with the extent of distal aortic calcification (0.76; 95%CI 0.60–0.97, p=0.02) but not proximal aortic calcification or proximal aortic distensibility (-0.04 $mmHg^{-1}$; 95%CI -0.16–0.09 $mmHg^{-1}$, p=0.60). Percent emphysema was associated with neither measure.

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DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

FEV_1 was associated with severity of distal aortic calcification where it was present independently of smoking and other cardiovascular risk factors but not with distensibility or calcification of the proximal aorta.

Keywords

forced expiratory volume; pulmonary emphysema; aorta; calcification; compliance

INTRODUCTION

Forced expiratory volume in one second strongly predicts mortality from cardiovascular disease in general population samples. (1) In addition, cardiovascular disease is an important cause of death in patients with chronic obstructive pulmonary disease (COPD) (2).

Pulse wave velocity (PWV), which predicts cardiovascular mortality, (3) is measured as the rate of transmission of a pressure wave across the aorta and femoral artery (4), and is thus an indirect measure of regional aortic stiffness. PWV is associated with FEV_1 in men, (5, 6) and is higher in COPD patients than in controls matched on age, sex and smoking. (7, 8) However, although regional aortic stiffness has been associated with pulmonary function we are not aware of any study examining the association between pulmonary function and local arterial stiffness within the aorta.

The highly elastic proximal aorta is rich in elastin and may therefore be susceptible to elastin degradation and abnormal collagen remodelling, whereas calcification of the more distal muscular aorta may arise from systemic inflammation and oxidative stress. As such proximal aortic pathology might implicate a common susceptibility in the connective tissue of artery and lung whereas distal aortic pathology might implicate systemic inflammation which is associated with airflow limitation. (9, 10) Abdominal aortic calcification is itself a strong predictor of cardiovascular mortality (11, 12) yet the relationship of FEV_1 to aortic calcification has not been established.

Therefore we tested the hypothesis that decrements in the FEV_1 and increments in percent emphysema on computed tomography (CT) scans are associated with reduced distensibility of the ascending aorta on magnetic resonance (MR) and calcification of the vasculature from the ascending aorta to the iliac arteries. (13)

METHODS

The Multi-Ethnic Study of Atherosclerosis (MESA) is a multicenter prospective cohort study designed to investigate sub-clinical cardiovascular disease in individuals without clinical cardiovascular disease. (14) In 2000–2002, MESA recruited 6,814 men and women ages 45–84 years old from six U.S. communities: Forsyth County, NC; Northern Manhattan and the Bronx, NY; Baltimore City and Baltimore County, MD; St. Paul, MN; Chicago, IL; and Los Angeles, CA. MESA participants were European-American white, African-American, Hispanic, or Asian-American (mostly of Chinese origin). Exclusion criteria were clinical cardiovascular disease, weight > 300 lbs, pregnancy or impediment to long-term participation. (14) MESA protocols and all studies described herein have been approved by the Institutional Review Boards of all collaborating institutions.

The MESA Lung Study enrolled 3,965 MESA participants of 4,483 sampled randomly from among those who consented to genetic analyses, underwent baseline measures of endothelial function, and attended an examination during the MESA-Lung recruitment period in 2004–

2006 (99%, 89%, and 91% of the MESA cohort, respectively). Chinese-Americans were over sampled to improve the precision of estimates for this group. For the current cross-sectional analysis related to obstructive lung disease, we excluded participants with restrictive spirometry, defined as a forced vital capacity (FVC) less than the lower limit of normal (LLN) (15) with a forced expiratory volume in one second (FEV_1)/FVC ratio above 0.70.

Aortic Calcification

CT scans of the abdomen were acquired on multidetector (MD) and electron beam (EBT) scans in 2002 and 2005 in a randomly selected subset of the cohort. CT images were analyzed centrally using a standard protocol by the MESA CT Reading Center. Calcification in the wall of the distal abdominal aorta in an 8 cm in length segment proximal to the aortic bifurcation was measured. For consistency with previous MESA studies, calcification was identified as a plaque of ≥1mm^2 with a density of ≥130 Hounsfield units (Hu) and quantified using the Agatston scoring method. (13) Calcification in the proximal abdominal aorta and each iliac artery was scored similarly.

Similar methods were used on cardiac CT scans in 2000–02 (16) to measure ascending aortic calcification and descending thoracic aortic calcification. Calcification was identified as plaque of ≥4.6 mm3 and ≥5.5 mm3 on EBT and MDCT respectively as previously described. (17)

Proximal Aortic Distensibility

Consenting participants underwent a cardiac MR scan in 2000–2002. The protocol, its reliability and characteristics of MESA participants with and without MR measures have been previously described. (18) All imaging was performed on 1.5 T magnets with a 4-element phased-array surface coil positioned anteriorly and posteriorly, electrocardiographic gating, and brachial artery blood pressure monitoring.

Aortic cross sectional area at the level of the right pulmonary artery during systole and diastole were calculated in a subset of the cohort using an automated contour routine using the software FLOW (Medis, Netherlands). Brachial blood pressure was measured with the participant supine in the MRI scanner before and after the scan. Proximal aortic distensibility, a well-validated measure of proximal aortic stiffness, (18, 4) was calculated as 1000 × (maximum area – minimum area) / (minimum area × brachial pulse pressure). (18) Left ventricular stroke volume was calculated as previously described. (19)

Spirometry

Spirometry was conducted in 2004–2006 in accordance with the American Thoracic Society/European Respiratory Society guidelines. (20) All participants performed at least three acceptable manoeuvres. Tests were conducted using a dry-rolling-sealed spirometer and software that performed automated quality checks as manoeuvres were performed (Occupational Marketing, Inc., Houston, TX). All spirometry exams were reviewed by one investigator and each test was graded for quality. (21) Participants with no acceptable curves were excluded from spirometry analyses.

CT Percent Emphysema

Quantitative measures of emphysema on CT scan were performed on the lung fields of full-inspiration cardiac CT scans acquired in 2000–2002, which imaged approximately 70% of the lung volume from the carina to the lung bases. (22) Two scans were performed on each participant; the scan with the higher air volume was used for analyses except in cases of discordant scan quality, in which case the higher quality scan was used.

Image attenuation was assessed using modified Pulmonary Analysis Software Suite (23) at a single reading centre by trained readers without knowledge of other participant information. CT percent emphysema low attenuation area was defined as the percentage of the total voxels in the lung which fell below −910 HU. The ICC on blinded re-reads was 0.94. Attenuation of inside and outside air was measured, and CT percent emphysema measures corrected for each were obtained for use in sensitivity analyses.

Percent emphysema measures from the carina to lung base are highly correlated (r=0.99) with full-lung measures on the same full-lung scans in smokers. Emphysema measures from MESA cardiac scans correlated with full-lung scans (e.g., r=0.93 on MD-CT scanners). (22)

Potential Confounders

Age, gender, race/ethnicity, educational attainment, and medical history were self-reported. Current smoking was defined as self-report of a cigarette in the last 30 days or urinary cotinine level at the time of CT exam of greater than 100 ng/ml (Immulite 2000 Nicotine Metabolite Assay; Diagnostic Products Corp., Los Angeles, CA).

Asthma was defined as self-report of physician-diagnosed asthma before age 45 years in order to avoid including participants with COPD in the definition of asthma, as misdiagnosis is common and differential by gender. (24)

Height, weight and resting blood pressure were measured using standard techniques, the latter with the Dinamap Monitor PRO 100 (Critikon, Tampa, FL) automated oscillometric device. Hypertension was defined as a systolic blood pressure > 140 mm Hg, a diastolic blood pressure > 90 mm Hg, or currently taking medications for BP control. (25)

Glucose and lipids were measured after a 12-h fast. The presence of diabetes mellitus was based on self-reported physician diagnosis, use of insulin and/or oral hypoglycaemic agent, or a fasting glucose value >126 mg/dL measured by rate reflectance spectrophotometry (Johnson & Johnson Clinical Diagnostics, Inc., Rochester, NY). Total cholesterol was measured using a cholesterol oxidase method (Roche Diagnostics), as was HDL after precipitation of non-HDL cholesterol with magnesium/dextran, triglycerides using Triglyceride GB reagent (Roche Diagnostics). LDL-cholesterol was calculated in plasma specimens having a triglyceride value <400 mg/dl using the formula of Friedewald et al.

Statistical Analysis

Demographics and medical characteristics were tabulated by respiratory condition/ spirometric criteria. Among individuals without self-reported asthma before age 45, participants with normal lung function and with various degrees of severity of severity of airflow obstruction were compared. Multiple linear regression of proximal aortic distensibility on lung density and lung function was performed. Analyses adjusted for study site, age, race/ethnicity, gender, height, body mass index, cigarette smoking status, pack years, diabetes, hypertension, educational attainment (as a measure of socioeconomic status), serum low density lipoprotein, high density lipoprotein, and glucose concentration, antihypertensive therapy, and lipid lowering therapy.

We employed relative risk regression with robust standard errors (log-link and Poisson error distribution) to estimate associations between relevant variables and the presence of detectable calcification. Among participants with detectable calcification we modelled the log-transformed magnitude of distal abdominal aortic calcification using linear regression. The exponentiated coefficients are presented, and may be interpreted as multiplicative (i.e. ratio) change in average distal abdominal aortic calcification. (26) Formal adjustments for

multiple comparisons were not performed, (27) but rather the results of all analyses are presented.

Sensitivity analyses were performed using emphysema measures corrected for both outside and inside air. Interactions were tested with multiplicative terms in regression models. Analyses were performed with SPSS version 14 (Chicago, Illinois, USA) and R 2.8.1 (R Foundation, Vienna, Austria). P-values were two-tailed with $p < 0.05$ considered statistically significant.

RESULTS

Of the participants in the MESA Lung Study with valid spirometry measures and without restrictive lung disease, 1,917 had proximal aortic distensibility MR measures and 1,312 had distal abdominal aortic CT measures (Figure 1). Those with proximal aortic distensibility MR measures were younger and less likely to have hypertension and diabetes but were otherwise similar to those without such measures. Participants with distal abdominal aortic calcification measures were very similar to those without.

Participants with proximal aortic distensibility measures were on average 60 years old and 47.1% were male. Nine percent reported a diagnosis of asthma before age 45 years, and 148 (7.7%) of the remaining participants had airflow obstruction on spirometry. Those with airflow obstruction were older, more likely to be male and to have hypertension, diabetes, chronic bronchitis and a history of smoking (Table 1). Similar associations were found for the sub-group with distal abdominal aortic calcification measures (Table 2).

Pulmonary Function in Relation to Aortic Calcification

Of the 1,312 participants who had distal abdominal aortic calcification measured, 903 (68.8%) had detectable calcification. Although the presence of distal abdominal aortic calcification was not associated with FEV_1 (RR 0.92; 95% CI 0.80 to 1.07; $p = 0.28$) lower FEV_1 was associated with a greater multiplicative (ratio) increment in the extent of distal abdominal aortic calcification after adjusting for study centre, age, sex, race/ethnicity, height, and BMI (FEV_1, 0.57, 95% CI, 0.45 to 0.72, $p<0.001$). The strength of the association was attenuated but still evident after additional adjustment for cigarette smoking status, pack years, diabetes, hypertension, educational attainment, serum low density lipoprotein, high density lipoprotein, and glucose concentration, antihypertensive therapy, and lipid lowering therapy (0.76, 95% CI 0.60 to 0.97, $p=0.02$).

The FEV_1/FVC ratio was also associated with the extent of distal abdominal aortic calcification after minimal adjustment, and similar trends were evident in the full model, although the associations were no longer statistically significant (Table 3).

Similar associations between FEV_1 and vascular calcification were found in the more distal iliac arteries (Figure 2). In contrast, there was no evidence for an association between FEV_1 and ascending aortic calcification or descending thoracic aortic calcification (Figure 2). A similar pattern was found for the FEV_1/FVC ratio, but not for the FVC (data not shown).

Pulmonary Function in Relation to Proximal Aortic Distensibility

Similar to findings for thoracic aortic calcification, proximal aortic distensibility was not associated with pulmonary function after adjusting for study center, age, sex, race/ethnicity, height, and BMI (-0.02 $mmHg^{-1}$, 95% CI -0.15 to 0.11 $mmHg^{-1}$, $p =0.75$) or after adjusting for the additional covariates as described above (-0.04, 95% CI -0.16 to 0.09, $p = 0.60$). Results for the FEV_1/FVC ratio were similarly null (Table 3).

CT Percent Emphysema in Relation to Proximal Aortic Distensibility, and Distal Abdominal Aortic Calcification

There was no evidence to suggest that CT percent emphysema was associated with abdominal aortic calcification (1.05, 95% CI 0.72 to 2.06, p=0.47) or aortic distensibility (0.03 $mmHg^{-1}$, 95% CI −0.02 to 0.09 $mmHg^{-1}$, p = 0.19) in the full multivariate models adjusted for study site, age, race/ethnicity, gender, height, body mass index, cigarette smoking status, pack years, diabetes, hypertension, educational attainment, serum low density lipoprotein, high density lipoprotein, and glucose concentration, antihypertensive therapy, lipid lowering therapy and scanner type and protocol.

Airflow Obstruction on Spirometry in Relation to Proximal Aortic Distensibility, and Distal abdominal aortic calcification

Similar results for distal abdominal aortic calcification were obtained when participants were compared by respiratory condition/spirometric criteria. Compared to participants with normal lung function without self-reported asthma, distal abdominal aortic calcification was higher for participants with moderate airflow obstruction (1.24, 95% CI 0.87 to 1.79), and higher still in those with severe airflow obstruction (1.31, 95% CI 0.55 to 3.13).

Reduced proximal aortic distensibility was not evident in participants with moderate or severe airflow obstruction, indeed compared to participants with normal lung function, proximal aortic distensibility was higher for those with moderate airflow obstruction (0.24 $mmHg^{-1}$, 95% CI 0.02 to 0.46 $mmHg^{-1}$) and severe airflow obstruction (0.09 $mmHg^{-1}$, 95% CI −0.44 to 0.62 $mmHg^{-1}$).

Sensitivity Analyses

Sensitivity analyses limited to participants who had smoked greater than 10, 20 and 50 pack-years produced similar results. Exclusion of participants with asthma diagnosed before the age of 45 did not affect the results; neither did exclusion of participants with any diagnosis of asthma, nor use of CT percent emphysema measures corrected for outside air or airways air, or use of the 15th percentile point. Additional adjustment for self-reported use of bronchodilators, steroids, or methylxanthines and measures of inflammation (serum interleukin-6 and C-reactive protein levels) had little impact on the results.

There was no evidence for effect modification on an additive scale by gender, race/ethnicity, smoking status, study site, CT scanner type or severity of airflow obstruction on spirometry, nor any evidence of statistically significant departures from linearity for any of the main relationships (data not shown).

DISCUSSION

In this unique and large study, an obstructive pattern of spirometry was associated with greater extent of calcification in the distal aorta. In contrast, obstructive spirometry was associated neither with proximal aortic calcification nor with proximal aortic distensibility on MRI. Furthermore, there was a graded increase in the magnitude of the association between pulmonary function and the extent of calcification from the proximal thoracic to distal abdominal aorta.

Previous population-based studies that have examined associations between pulmonary function and PWV are limited to two European studies of 194 and 827 middle aged men, (6) in which associations were found, and one negative study in 678 healthy Japanese-Americans. (28) Aortic PWV has also previously been found to be higher in patients with COPD than controls matched on age, sex and smoking. (7, 8)

Abdominal aortic calcification is associated with PWV. (29, 30) and, like PWV, is a cardiovascular risk factor (11, 12). Therefore, it is of some interest that calcification is related to pulmonary function. Our study adds to the literature by demonstrating that pathological changes in the distal aorta are more likely to explain the association between pulmonary function and aortic stiffness than changes in the proximal aorta.

These findings may generalise to patients with COPD as, despite loss of statistical power as a consequence of categorisation, similar results for abdominal aortic calcification and proximal aortic distensibility were obtained when participants were compared by respiratory condition, as defined spirometrically.

The mechanisms underlying the distal aortic calcification are unknown, but inflammatory mediators such as TNF-alpha, high sensitivity C-reactive protein and oxidised lipids, which are increased in COPD, (9, 31) could mediate an association between impaired lung function and vascular calcification which occurs both in the intima in atheromatous plaques, and in the medial elastic laminae. C-reactive protein has been implicated in atheroma formation. (32) TNF-alpha causes smooth muscle cells to undergo osteoblastic differentiation and mineralisation thereby promoting calcification. (33) Oxidised lipids also promote smooth muscle cell osteoblastic differentiation, but inhibit this process in bone-derived preosteoblasts (34) which is of particular interest since osteoporosis is inversely associated with arterial stiffness in COPD. (7)

We did not find any attenuation in the association between FEV_1 and abdominal aortic calcification after adjusting for C-reactive protein and interleukin-6. However, both measures show considerable variability and were only measured at a single time point, while measures of TNF-alpha and oxidised lipids were not available for the majority of participants.

Comprehensive assessments meant that we were able to adjust for a wide range of potential confounders including cigarette smoke exposure and cardiovascular risk factors, although we did not measure arterial oxygen tension. Nevertheless, acute changes in oxygenation appear unlikely to affect vascular calcification.

Spirometry was performed without administering a bronchodilator, and as such a proportion of participants with airflow obstruction may have had asthma. However, excluding participants who had ever had a diagnosis of asthma did not affect our findings, nor did confining the analysis to those participants with a 50 or greater pack year smoking history. Moreover, participants with asthma had higher aortic distensibity and lower calcification.

MESA CT measures of emphysema were obtained from the lung fields of cardiac CT scans and therefore visualization of the lung apices was limited. Nonetheless, the CT percent emphysema measures were highly reproducible and validated. (22)

Lung function was assessed approximately 4 years after the other measures. However, the expected mean change in FEV_1 over a period of 4 years in a population-based study such as MESA is small, (35) and in a previous population-based study aortic PWV was found to be associated with FEV_1 measured approximately 10 years prior as well as FEV_1 measured contemporaneously, suggesting that relationships between pulmonary function and aortic stiffness are reasonably consistent over time. (6)

MESA excluded participants with known cardiovascular disease at baseline. However, this is likely to lead to an underestimation of the strength of the association between aortic calcification and FEV_1.

Power was limited for participants with severe airflow obstruction, and caution is required in extrapolating these findings to this group. Nevertheless, there was no evidence for any departure from linearity across the range of lung function, and results comparing participants with moderate and severe airflow obstruction on spirometry were consistent with those obtained measuring pulmonary function in the full cohort.

CONCLUSION

In conclusion, FEV_1 was associated with distal aortic calcification where it was present independently of smoking and other cardiovascular risk factors but not with distensibility or calcification of the proximal aorta. Therefore pathological changes in the distal aorta are more likely to explain the association between pulmonary function and aortic stiffness than changes in the proximal aorta.

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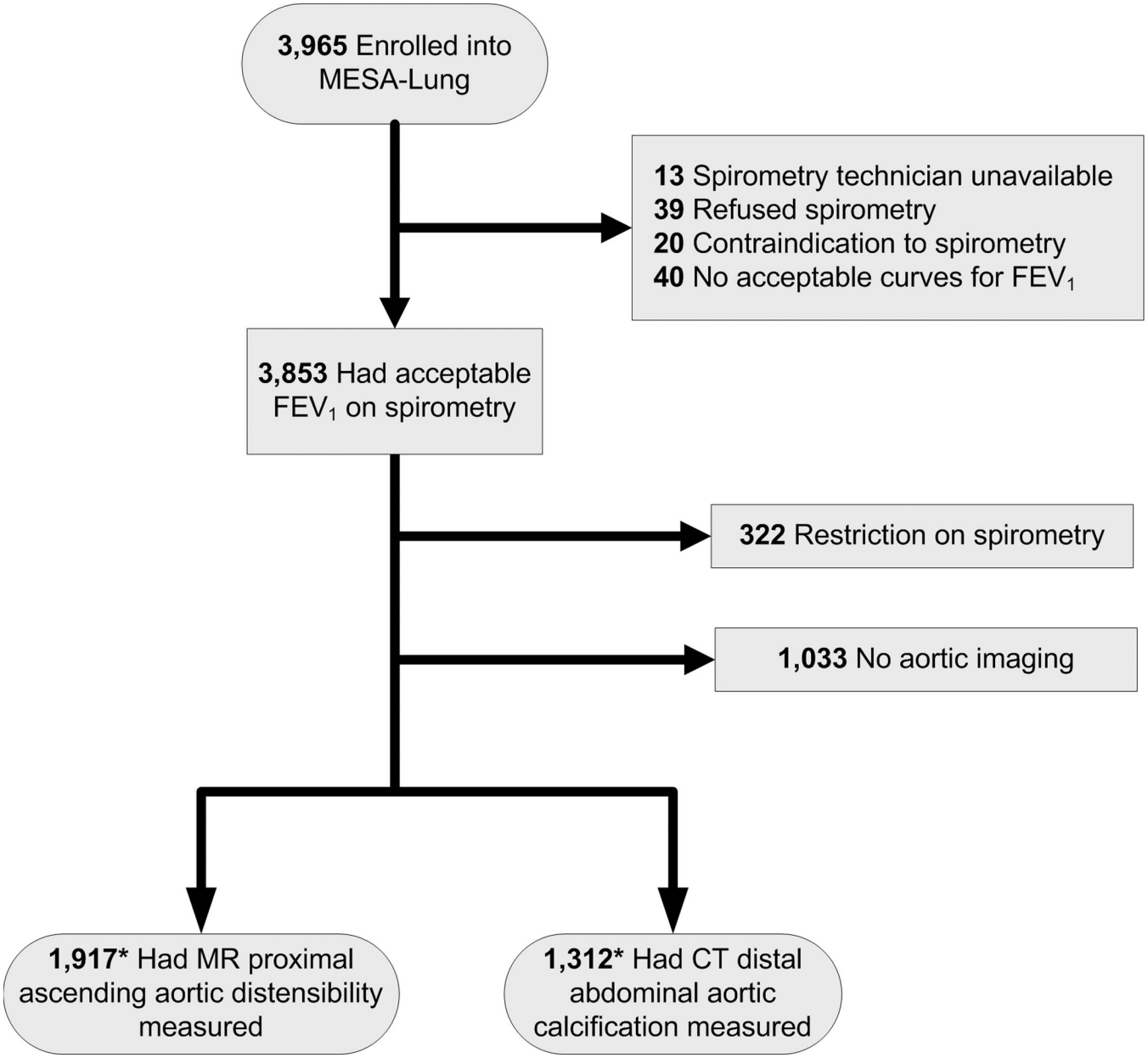

Figure 1.
Inclusion and exclusion criteria for cross-sectional analysis

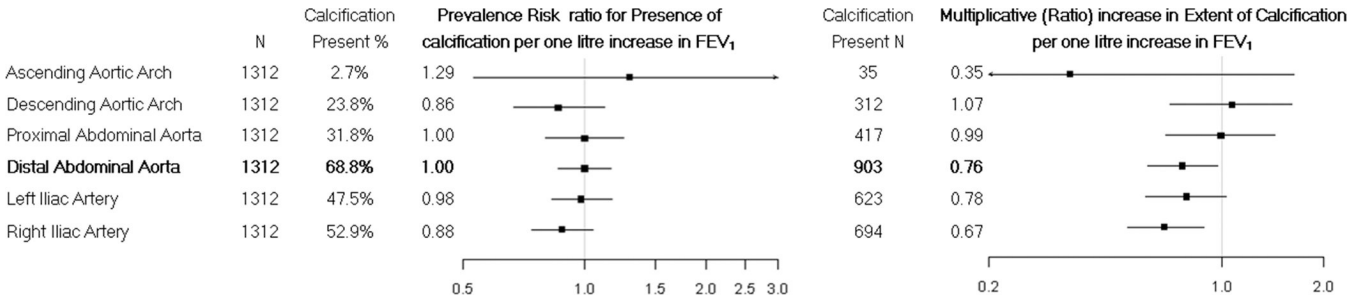

Figure 2.

Multivariate associations of the forced expiratory volume in one second with presence and multiplicative change in aortic calcification from the proximal ascending thoracic aorta to the distal abdominal aorta and iliac arteries

Table 1

Characteristics of Participants with Proximal Aortic Distensibility Measures, Stratified by Respiratory Status/Condition

			$FEV_1/FVC < 70\%$ without self-reported asthma		
	Normal spirometry without self-reported asthma	**Self-reported Asthma aged<45 years**	**FEV_1% predicted ≥ 80%**	**FEV_1% predicted 50% to 80%**	**FEV_1% predicted ≤ 50%**
N	1375	164	230	128	20
Age, mean (SD), years	59 (9)	58 (10)	66 (10)	63 (9)	65 (7)
Gender – male, n (%)	606 (44.1)	67 (40.9)	149 (64.8)	68 (53.1)	13 (65)
Height, mean (SD), cm	166 (10)	167 (10)	170 (10)	169 (10)	168 (10)
BMI, mean (SD), kg/m2	28 (5)	28 (5)	26 (4)	26 (4)	29 (6)
Ethnicity, n (%)					
Caucasian	461 (33.5)	70 (42.7)	118 (51.3)	66 (51.6)	7 (35)
Chinese	248 (18.0)	15 (9.1)	29 (12.6)	9 (7.0)	3 (16)
African-American	397 (28.9)	50 (30.5)	59 (25.7)	38 (29.7)	5 (25)
Hispanic	269 (19.6)	29 (17.7)	24 (10.4)	15 (11.7)	5 (25)
Smoking status, n (%)					
Never Smoked	733 (53.3)	87 (53.0)	90 (39.1)	33 (25.8)	1 (5)
Ex-smoker	488 (33.5)	55 (33.5)	106 (46.1)	60 (46.9)	9 (45)
Current Smoker	154 (11.2)	22 (13.4)	34 (14.8)	35 (27.3)	10 (50)
Pack Years, median (IQR)	15 (6–32)	15 (6–28)	24 (11–47)	29 (14–47)	52 (27–68)
Spirometry, mean (SD), %					
FEV_1 percent predicted	100 (14)	85 (18)	96 (11)	70 (9)	40 (9)
FVC percent predicted	98 (13)	94 (16)	109 (13)	86 (12)	67 (16)
FEV_1/FVC ratio	79 (5)	70 (10)	66 (4)	62 (7)	47 (13)
MRC Chronic Bronchitis, n (%)	92 (6.7)	26 (15.9)	18 (7.8)	12 (9.5)	6 (30.0)
CT Percentage Emphysema, median (IQR), %	13.6 (6.98–22.4)	17.4 (9.8–27.4)	25.1 (14.6–35.5)	18.4 (9.8–31.8)	27.0 (9.9–33.1)
Self reported, n (%)					
Hypertension	519 (37.7)	62 (37.8)	90 (39.1)	58 (45.3)	9 (45)
Diabetes	119 (8.7)	10 (6.1)	13 (5.7)	12 (9.4)	5 (25)
Antihypertensive medication	437 (31.8)	54 (32.9)	77 (33.5)	50 (39.1)	9 (45)
Lipid Lowering Therapy	197 (14.3)	21 (12.8)	39 (17.0)	17 (13.3)	4 (20)

			$FEV_1/FVC < 70\%$ without self-reported asthma		
	Normal spirometry without self-reported asthma	**Self-reported Asthma aged<45 years**	**FEV_1% predicted ≥ 80%**	**FEV_1% predicted 50% to 80%**	**FEV_1% predicted ≤ 50%**
BP, mean (SD), mmHg					
Systolic Blood Pressure	123 (19)	123 (19)	123 (19)	122 (20)	128 (16)
Diastolic Blood Pressure	72 (10)	72 (9)	71 (10)	70 (11)	72 (8)
Pulse Pressure	51 (15)	51 (16)	52 (15)	52 (15)	56 (13)
Heart Rate, mean (SD), beats/min	63 (9)	63 (8)	60 (9)	62 (10)	69 (14)
Lipids, mean (SD), mg/dl					
LDL Cholesterol	119 (29)	116 (33)	114 (30)	115 (32)	116 (29)
HDL Cholesterol	52 (15)	53 (15)	51 (15)	51 (15)	46 (9)
Triglycerides	129 (93)	128 (81)	109 (56)	124 (97)	136 (61)
C-Reactive Protein, median (IQR), mg/L	1.61 (0.72–3.69)	1.79 (0.76–3.29)	1.50 (0.57–3.29)	2.09 (0.77–4.89)	5.18 (1.11–7.35)

FEV_1 – Forced Expiratory Volume in One Second, FVC – Forced Vital Capacity, LDL – Low Density Lipoprotein, HDL – High Density Lipoprotein, BMI – Body Mass Index

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Table 2

Characteristics of Participants with Distal abdominal aortic calcification Measures, Stratified by Respiratory Status/Condition

			$FEV_1/FVC < 70\%$ without self-reported asthma		
	Normal	**Self-reported Asthma aged<45**	**FEV_1% predicted ≥ 80%**	**FEV_1% predicted 50% to 80%**	**FEV_1% predicted ≤ 50%**
N	939	89	161	108	15
Age, mean (SD), years	60 (9)	60 (10)	67 (9)	64 (9)	67 (7)
Gender – male, n (%)	455 (48.5)	41 (46.1)	105 (65.2)	61 (56.5)	14 (93)
Height, mean (SD), cm	166 (10)	167 (10)	170 (10)	170 (11)	174 (6)
BMI, mean (SD), kg/m2	28 (5)	29 (5)	26 (4)	28 (5)	28 (4)
Ethnicity, n (%)					
Caucasian	338 (36.0)	46 (51.7)	84 (52.2)	56 (51.9)	8 (53)
Chinese	163 (17.4)	6 (6.7)	26 (16.1)	10 (9.3)	1 (7)
African-American	176 (18.7)	18 (20.2)	29 (18.0)	25 (23.1)	3 (20)
Hispanic	262 (27.9)	19 (21.3)	22 (13.7)	17 (15.7)	3 (20)
Smoking status, n (%)					
Never Smoked	490 (52.2)	42 (47.2)	63 (39.1)	28 (25.9)	1 (7)
Ex-smoker	331 (35.3)	35 (39.3)	72 (44.7)	46 (42.6)	6 (40)
Current Smoker	118 (12.6)	12 (13.5)	26 (16.1)	34 (31.5)	8 (53)
Pack Years, median (IQR)	15 (6–32)	19 (9–36)	27 (14–50)	28 (14–45)	62 (49–85)
Spirometry, mean (SD), %					
FEV_1 percent predicted	101 (13)	83 (19)	96 (13)	69 (9)	39 (9)
FVC percent predicted	99 (12)	90(14)	109 (14)	83 (11)	73 (18)
FEV_1/FVC ratio	78 (5)	69 (11)	66 (4)	63 (6)	41 (12)
MRC Chronic Bronchitis, n (%)	67 (7.2)	18 (20.2)	15 (9.3)	7 (6.5)	7 (47)
CT Percentage Emphysema, median (IQR), %	13.6 (6.98–22.4)	17.4 (9.8–27.4)	25.1 (14.6–35.5)	18.4 (9.8–31.8)	27.0 (9.9–33.1)
Self reported, n (%)					
Hypertension	368 (39.2)	40 (44.9)	71 (44.1)	50 (46.3)	6 (40)
Diabetes	92 (9.8)	8 (9.0)	11 (6.8)	9 (8.3)	3 (20)
Antihypertensive medication	291 (31)	34 (38.2)	48 (29.8)	41 (38)	6 (40)
Lipid Lowering Therapy	146 (15.6)	13 (14.6)	32 (19.9)	13 (12)	3 (20)
BP, mean (SD), mmHg					

			$FEV_1/FVC < 70\%$ without self-reported asthma		
	Normal	**Self-reported Asthma aged<45**	**FEV_1% predicted ≥ 80%**	**FEV_1% predicted 50% to 80%**	**FEV_1% predicted ≤ 50%**
Systolic Blood Pressure	124 (19)	128 (19)	127 (22)	125 (20)	121 (12)
Diastolic Blood Pressure	72 (10)	74 (9)	73 (11)	72 (10)	73 (6)
Pulse Pressure	52 (16)	54 (16)	54 (17)	53 (16)	48 (9)
Heart Rate, mean (SD), beats/min	63 (9)	64 (8)	61 (8)	64 (9)	69 (13)
Lipids, mean (SD), mg/dl					
LDL Cholesterol	119 (30)	117 (32)	115 (26)	117 (32)	120 (34)
HDL Cholesterol	51 (15)	51 (14)	53 (18)	50 (14)	45 (8)
Triglycerides	132 (76)	133 (79)	126 (86)	138 (103)	111 (50)
C-Reactive Protein, median (IQR), mg/L	1.62 (0.73–3.78)	1.89 (0.77–3.66)	1.39 (0.65–2.96)	2.41 (1.02–4.51)	4.29 (1.82–7.09)

FEV_1 – Forced Expiratory Volume in One Second, FVC – Forced Vital Capacity, LDL – Low Density Lipoprotein, HDL – High Density Lipoprotein, BMI – Body Mass Index

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Table 3

Multivariate Analysis – Distal abdominal aortic calcification and Proximal Aortic Distensibility in Relation to FEV_1, FVC, the FEV_1/FVC ratio, and CT Percent Emphysema

Exposure (units)	Estimated multiplicative (ratio) change in distal abdominal aortic calcification (95% CI), n=903	P Value for Trend	Absolute change in proximal aortic distensibility ($mmHg^{-1}$), (95% CI), n=1917	P value
FEV_1 (litres)				
Model 1	0.57 (0.45 to 0.72)	<0.001	−0.02 (−0.15 to 0.11)	0.75
Model 2	0.76 (0.60 to 0.97)	0.02	−0.04 (−0.16 to 0.09)	0.60
FVC (litres)				
Model 1	0.72 (0.58 to 0.91)	0.006	0.02 (−0.09 to 0.13)	0.29
Model 2	0.82 (0.66 to 1.02)	0.07	0.00 (−0.88 to 0.45)	0.95
FEV_1/FVC (ratio)				
Model 1	0.76 (0.67 to 0.86)	<0.001	−0.35 (−1.00 to 0.30)	0.30
Model 2	0.91 (0.80 to 1.04)	0.17	−0.21 (−0.88 to 0.45)	0.53

FEV_1 – Forced Expiratory Volume in One Second, FVC – Forced Vital Capacity

Model 1: adjusted for study site, age, race/ethnicity, gender, height, and body mass index.

Model 2: adjusted for model 1 and cigarette smoking status, pack years, diabetes, hypertension, educational attainment, serum low density lipoprotein, high density lipoprotein, and glucose concentration, antihypertensive therapy, and lipid lowering therapy.